

Glycosyltransferase ST6GAL1 contributes to the regulation of pluripotency in human pluripotent stem cells.

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Public Summary:

Many studies have suggested the significance of glycosyltransferase-mediated macromolecule glycosylation in the regulation of pluripotent states in human pluripotent stem cells (hPSCs). Here, we observed that the sialyltransferase ST6GAL1 was preferentially expressed in undifferentiated hPSCs compared to non-pluripotent cells. A lectin which preferentially recognizes α -2,6 sialylated galactosides showed strong binding reactivity with undifferentiated hPSCs and their glycoproteins, and did so to a much lesser extent with differentiated cells. In addition, downregulation of ST6GAL1 in undifferentiated hPSCs led to a decrease in POU5F1 (also known as OCT4) protein and significantly altered the expression of many genes that orchestrate cell morphogenesis during differentiation. The induction of cellular pluripotency in somatic cells was substantially impeded by the shRNA-mediated suppression of ST6GAL1, partially through interference with the expression of endogenous POU5F1 and SOX2. Targeting ST6GAL1 activity with a sialyltransferase inhibitor during cell reprogramming resulted in a dose-dependent reduction in the generation of human induced pluripotent stem cells (hiPSCs). Collectively, our data indicate that ST6GAL1 plays an important role in the regulation of pluripotency and differentiation in hPSCs, and the pluripotent state in human cells can be modulated using pharmacological tools to target sialyltransferase activity.

Scientific Abstract:

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